Remarks

After amendment, claims 40, 51-56 and 67 remain pending in the present application. Claims 50 has been amended. Claim 66 has been canceled. The subject matter of claim 66 has been amended and newly presented in claim 67. Claims 57-65 and claims 1-39 have been cancelled previously *without prejudice*. Support for the amendment to the claims can be found throughout the originally filed application and claims and in particular, for newly presented claim 67, on page 11, line 3. No new matter has been added by way of this amendment.

Applicants note that any subject matter which is cancelled herein, including any subject matter canceled from previously pending claims is made *without prejudice* in order to give Applicant a chance to consider filing any one or more divisional/continuation applications to seek allowance of that subject matter. The present amendments have been made to expedite allowance of the instant application and in particular, to address the enablement issue associated with cancers that are other than solid tumors. The presently pending claims are now directed to the use of the compounds as claimed in treating solid tumors and cancers as otherwise set forth in the claims. The treatment of the claimed tumors/cancers as set forth in the claims is consistent with the activity of the claimed compounds as anti-angiogenesis agents. The accompanying declaration of Dr. Jack Arbiser is enclosed in support of the enablement of the present invention. The attached declaration outlines cell-based assays performed on benign tumor cells (FP52 SV40) and malignant sarcoma cells (TSC2ang1) using solenopsin to test its anti-proliferative and/or anti-cancer activity. The assays evidenced that solenopsin exhibits substantial antiproliferative activity in both cells assays which is consistent with its use as an anticancer agent as is claimed.

Rejections

The Examiner has objected to or rejected the previously pending claims 40, 50-56 and 66 variously under 37 C.F.R. §1.75(c) and 35 U.S.C. §112, first and second

paragraphs for the reasons which are stated in the October 28, 2010 office action on pages 2-7. Applicants respectfully submit that the presently pending claims are in conformance with the requirements of 37 C.F.R. and 35 U.S.C. and are in condition for allowance for the reasons which are presented hereinabelow.

The Objection to Claims 50 and 51 Under 37 C.F.R. §1.75(c)

The Examiner has rejected previously pending claim 50 as being of improper dependent form for failing to further limit the subject matter of a previous claim. In particular, the Examiner contends that claim 50 repeats the identical options for the tumor which are recited by amended claim 40. Applicants have amended claim 50 accordingly and assert that claim 50 is now properly dependent on claim 40 in compliance with the requirements of 37 C.F.R.

The §112, Second Paragraph Rejection

The Examiner has rejected previously pending claim 60 35 U.S.C. §112, Second Paragraph for the reasons which are presented in the June, 2010 office action on page 9. In response, Applicants have deleted claim 60 (66) and replaced amended claim 66 with new claim 67. New claim 67 indicates that the basal cell carcinoma or the squamous cell carcinoma set forth in claim 40 is a cutaneous malignancy. Applicants respectfully submit that claim 67 fully complies with the requirements of 35 U.S.C. §112, second paragraph.

The §112, First Paragraph Rejection

The Examiner has rejected/objected to previously pending claims 40, 51-56 and 66 under 35 U.S.C. §112, first paragraph as being non-enabled for tumors and cancers which are presently claimed in the instant application as stated in the office action on pages 3-7. In particular, the Examiner indicates that the previously pending claims are directed to the treatment of a number of tumors and cancer for which enablement of the

present invention is not provided. In response, Applicants had attached the declaration of Dr. Jack L. Arbiser, M.D., Ph.D. in support of patentability of the present invention. Dr. Arbiser, who has extensive experience in cancer/tumor chemotherapy provided evidence that the presently claimed compounds are anti-angiogenesis inhibitors and as such, display an activity which is consistent with the generic therapy of tumors and cancer. Based upon the previously enclosed declaration of Dr. Arbiser, and the references cited therein (copies of which were submitted to the Patent Office on October 5, 2010-additional copies attached hereto, as well as receipts confirming receipt by the Patent Office), Applicants respectfully submit that the presently claimed invention is enabled and therefore, patentable.

The two papers previously submitted (as evidenced by receipt from the Patent Office), Arbiser, et al., ***Blood,*** 15 January 2007 109, 2, 560-565 ("Arbiser") and Park, et al., ***Journal of Infectious Diseases,*** 15 October 2008, 198, 1198-201 ("Park") and again submitted herewith, evidence that the claimed compounds are inhibitors of phosphatidyl-3-kinase (Arbiser) and because of the small molecular size and stability of solenopsin, as evidenced by both Arbiser and Park, these characteristics make the compound amenable to topical, systemic and oral administration, and an attractive molecule for the treatment of tumors and cancer. As indicated by combined teachings of the Arbiser and Park references, and as set forth in Dr. Arbiser's attached declaration, solenopsin thus represents close to an ideal compound for providing generic therapy against a variety of cancerous tissue and its use as an anticancer agent is consistent with its activity as an inhibitor of angiogenesis, given that inhibitors of phosphatidyl-3-kinase activity exhibit anti-angiogenesis activity. See Arbiser, supra.

It is noted that the solenopsin compounds which are set forth in the presently claimed methods exhibit exceptional activity as inhibitors of phosphatidylinositol-3 kinase, and consequently, both directly and indirectly inhibit angiogenesis, which is critical for tumor/cancer growth and elaboration. Dr. Arbiser presents evidence in the form of two papers from his laboratory, in particular, Arbiser, et al, *Blood*, 15 January 2007, Volume 109, Number 2, pages 560-565 and Park, et al., *Journal of Infectious*

Diseases, 15 October 2008, 198, 1198-201, attached hereto. The first reference, Arbiser, evidences that solenopsin is an effective inhibitor of phosphatidylinositol-3 kinase and consequently angiogenesis and the second reference evidences that solenopsin is a stable compound and may be used consistent with its presentation as a pharmaceutical agent.

By virtue of the inhibition which is implicated in both the direct and indirect inhibition of angiogenesis and the fact that inhibition of angiogenesis is consistent with favorable therapeutic outcomes in a variety of tumors and cancer, Dr. Arbiser concludes that it is his expectation as a person of extraordinary experience and skill in cancer treatment modalities, that the present invention will be generally applicable for favorable therapeutic intervention and the treatment of a broad range of tumors and cancer as claimed. This expectation is further born out by the experimental evidence obtained from cell based assays conducted under Dr. Arbiser's supervision and control, which tested the inhibition of solenopsin on the proliferation of cells from a benign tumor (FP52 SV40) and malignant sarcoma (TSC2ang1), described in the attached declaration of Dr. Arbiser, in paragraphs 29-30. In each of the assays, as described in the Arbiser declaration, solenopsin evidenced substantial anti-proliferative activity consistent with its use as an anticancer agent as presently claimed in the present application.

As a separate matter, Applicants have evidenced that the present application enables the present invention as it relates to making and using the invention without engaging in undue experimentation. In particular, the present specification clearly indicates the chemical compounds which are used in the present invention, provides for the syntheses of the compounds, some of which are readily available in the literature, and provides for pharmaceutical formulations which are readily prepared using known methods and pharmaceutically acceptable carriers, additives and excipients as indicated in the specification. The specification provides that effective amounts or concentrations of compounds as claimed are used in the present invention and provides, on page 15, guidelines as to the amounts or concentrations of compounds which are to be used in the pharmaceutical compositions according to the present invention. The specific disclosure in the present application, which provides for the treatment of a tumor or cancer using an

effective amount of the compounds as claimed is clearly enabled. Making routine changes to the delivery of the compounds in treating a variety of cancers which rely on the generic mechanism of inhibition of angiogenesis in cancer cells and tissue to effect treatment is well within the skill of the routineer and does not amount in any way to undue experimentation. The specification, coupled with the Arbiser and Park paper provided, as well as the experimental evidence presented in the attached Arbiser declaration fully support Applicants' view that their invention may be used by the person of ordinary skill without engaging in undue experimentation in conformity with 35 U.S.C. §112, first paragraph.

Based upon the attached declaration of Dr. Arbiser, the references attached thereto and the experimental evidence which is presented in the declaration, and as otherwise provided in the present application, Applicants respectfully submit that the presently claimed invention meets the requirements of 35 U.S.C. §112, first paragraph.

No other rejections of the previously pending claims were made by the Examiner.

Information Disclosure Statement

With respect to the previously submitted information disclosure statement which was filed electronically September 28, 2010, but apparently not considered by the Examiner because a fee was due for submission and not presented, Applicants respectfully submit that throughout the papers of this application, from the original filing of the application through each submission of a response in the present application, the Commissioner was authorized to charge any fee due to Deposit Account 04-0838. Applicants respectfully submit that pursuant to the various statements authorizing the debiting of any fee due to the Deposit Account, if the Examiner decided that a fee was due for submission of the Information Disclosure Statement, the debiting of such fee to the Deposit Account would have been considered proper. Indeed, the debiting of the Deposit Account for any fee due was further requested in the response filed October 4, 2010, a week after the Information Disclosure Statement was filed electronically. In light of the oversight, Applicants respectfully request that the Examiner now consider the

Information Disclosure Statement previously filed September 28, 2010 and to debit any fee due for consideration of the Information Disclosure Statement to Deposit Account 04-0838.

For all of the reasons which are set forth hereinabove, Applicants respectfully submit that the application is in condition for allowance and early action resulting in allowance of the instant application is earnestly solicited.

No fee is due for the presentation of this amendment. A petition for an extension of time is enclosed as is a notice of appeal and authorization to charge the petition fee of $65 and notice of appeal fee of $270 to Deposit Account 04-0838 is provided. Please charge any fee due or credit any overpayment previously made to Deposit Account No. 04-0838.

Respectfully submitted,

Dated: February 24, 2011
Enclosures: Arbiser Declaration w/Exhibits;
Arbiser and Park References

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Certificate of Facsimile Transmission

I hereby certify that this correspondence is being sent by facsimile to Examiner Brian M. Gulledge, in Group Art Unit 1612 of the United States Patent Office in Alexandria, VA 22313-1450 on February 28, 2011.

Henry D. Coleman, Reg. No. 32,559